REMARKS

The Amendments

Claim 3 is amended to correct an obvious typographical error. Claim 18 and claims dependent thereon are canceled pursuant to the restriction requirement. Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments. The amendments do not narrow the scope of the claims and/or were not made for reasons related to patentability. The amendments should not be interpreted as an acquiescence to any objection or rejection made in this application.

To the extent that the amendments avoid the prior art or for other reasons related to patentability, competitors are warned that the amendments are not intended to and do not limit the scope of equivalents which may be asserted on subject matter outside the literal scope of any patented claims but not anticipated or rendered obvious by the prior art or otherwise unpatentable to applicants.

The Restriction Requirement

Regarding claim 18, and claims dependent thereon, applicants' withdrawal their traversal of the restriction and these claims are canceled.

Regarding claim 1 and claims dependent thereon, applicants maintain their traversal of the restriction for the reasons previously given which are emphasized and supplemented as follows.

Applicants reiterate their objection to characterizing the subject matter all within the same generic claim 1 to cover a number of unrelated inventions. Apparently, the restriction

is being made based on the allegation that a method using one type of a "substance which eliminates or prevents formation of the cells of the undesired tissue" is "unrelated" to the same method with a different type of such substance. The Office Action alleges that inventions are "unrelated" if they have different functions, different effects or different modes of operation. And it is alleged that, apparently, any difference in the type of "substance which eliminates or prevents formation of the cells of the undesired tissue" results in a different mode of operation. Applicants urge that the wrong PTO practice regarding "unrelated inventions" is being applied and further that it is not being applied in a reasonable manner.

The standard being applied to support the restriction based on inventions being "unrelated" is taken from MPEP §806.04. However, this section does not relate to the instant fact situation. The part of MPEP §806.04 containing the language relied on in the Office Action states:

> (A) Two different combinations, not disclosed as capable of use together, having different modes of operation, different functions or different effects are independent. An article of apparel such as a shoe, and a locomotive bearing would be an example. A process of painting a house and a process of boring a well would be a second example.

This is clearly not the applicable section for the instant claims. There are not "two different combinations" involved here and the instant facts are nowhere near the type of situation of the examples given. Instead, the instant facts clearly relate to a genus-species situation, i.e., all the "substances" which are being restricted from one another are within the genus of a "substance which eliminates or prevents formation of the cells of the undesired tissue." Applicants strongly urge that, if the restriction is to be maintained, the Examiner identify what are the "two different combinations" which give rise to the restriction. Because

there are not two different combinations, the fact situation is governed by the genus-species practice, as follows:

> Where inventions as disclosed and claimed are both (A) species under a claimed genus and (B) related, then the question of restriction must be determined by both the practice applicable to election of species and the practice applicable to other types of restrictions such as those covered in MPEP § 806.05 -§ 806.05(i). If restriction is improper under either practice, it should not be required.

It is noted that none of the situations under MPEP § 806.05 -§ 806.05(i) apply here. Thus, only election of species practice would be proper.

Further, it is urged that, in any event, the standard is being unreasonably applied. Under the theory of the restriction, every species of every genus would always be restricted from each other. Every compound works somewhat differently from even closely related compounds. But this is not the basis for stating that they show a different mode of operation. Instant claim 1 sets forth the function that shows the substances all have the same general mode of operation, i.e., they eliminate or prevent formation of the cells of the undesired tissue.

It is not improper to define the substance according to its function. This is especially the case here, since the novelty of the invention does not lie in the particular substance used but in the manner of its local administration and local effect. This should be evident from the arguments on novelty/nonobviousness below. The claims are not merely to any method of "eliminating or reducing normal but undesired tissue in a patient" but only those methods which comprise the clearly defined and distinct steps of "administering a controlled release formulation to the patient by injection at a local area containing the undesired tissue such that the undesired tissue in the local area is eliminated or reduced, said formulation comprising a substance which eliminates or prevents formation of the cells of the undesired tissue, said

substance being provided in a controlled release carrier."

For all of the above reasons, withdrawal of the restriction requirement is earnestly requested. Claim 1 defines a proper Markush group and the claims should, at most, be subject to an election of species requirement and examination under the PTO's Markush practice.

The Claim Objection

The objection to claim 3 is rendered moot by the above amendment.

The Rejection under 35 U.S.C. §112, second paragraph

The rejection of claims 1-3, 5-12, 14-17 and 24-26 under 35 U.S.C. §112, second paragraph is respectfully traversed. It is alleged in the Office Action that one of ordinary skill in the art would not understand the meaning of "local area," as used in the applicants' claims.

Applicants respectfully submit that the meaning and the metes and bounds of the term "a local area containing the undesired tissue" used in claim 1 would have been well understood by one of ordinary skill in the art and that the meaning of the claim would be sufficiently clear to one of ordinary skill in the art. The specification gives clear guidance to one of ordinary skill in the art as to the meaning of the term and the term would be further understood by its standard usage in this art. First, the claim itself helps to define the "local area" term since it specifies that it is "a local area containing the undesired tissue." The extent of the undesired tissue is well definable and, thus, a local area within such extent is well definable also. Second, the specification gives ample guidance as to the meaning of the term. The specification distinguishes the inventive local administration from general

administration in the Background section of the specification. Also in the Background, it points out other art which utilize local administration methods for different effects. Thus, it is clear that local administration is a term used in the art having a defined meaning. Further, the specification gives representative examples of specific types of administration to achieve the local area treatment (see, e.g., page 6, third full paragraph, and paragraph bridging pages 6-7). Finally, the specification provides in vivo and in vitro examples with rat models demonstrating specific applications of the method and showing their localized effect (see pages 8-18 of the specification). Additionally, as exemplified by the art cited by applicants in the specification, the term "local area" would be understood to have a particular meaning to those skilled in the art of administration of drugs. It is well understood in this art that a "local area" defines treatment of a discrete area of the body and is distinguished from treatments which affect the body as a whole. See, e.g., the definition of "local" in the attached excerpt from the "International Dictionary of Medicine and Biology" vol. II (1986).

The standard for definiteness is set forth in terms of reasonableness and in terms of consideration of both the prior art and the description provided in the application, see, e.g., *In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236 (CCPA 1971). Thus, the claims need not be absolutely definite but are acceptable when reasonably definite to one of ordinary skill in the art. See also, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1986). For all of the above reasons, it is urged that the "local area" term would have been reasonably definite to one of ordinary skill in the art and the rejection under 35 U.S.C. §112, second paragraph, should be withdrawn.

The Rejection under 35 U.S.C. §112, first paragraph

The rejection of claims 1-3, 5-12, 14 and 17 under 35 U.S.C. §112, first paragraph, is

respectfully traversed.

The rejection appears to be largely made on the basis that the claims are allegedly too broad. However, breadth alone is not a sufficient basis for a rejection under 35 U.S.C. §112, first paragraph. Undue breadth is only the basis for rejection for lack of written description where the claims recite subject matter broader than what is described in the original disclosure. That is, obviously, not the situation here since the claims in question here are the original claims and, thus, by definition are exactly described in the original disclosure.

The MPEP (§2163 (I)(A)) states under the section addressing original claims (which is the case here): "There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)." Although the law allows for instances wherein original claims still lack adequate written description, none of the examples of such given in the MPEP are based on the claims being allegedly overbroad. None of the examples given in the MPEP are analogous to the instant facts. Further, the MPEP guidelines for analyzing 35 U.S.C. §112, first paragraph, written description issues, see, e.g., §2163 (II)(3), refers to the standard where original claims are involved and indicates a showing of a reduction to practice can evidence possession of the invention. In fact, the specification here does provide a reduction to practice of the invention. The in vivo rat model examples of the disclosure evidence a clear reduction to practice – and thus possession – of the invention by the applicants.

The Office Action alleges that the examples in the specification are insufficient to support the genus of tissue types treated for removal and the genus of compounds used to effect such removal encompassed by the claims. However, the standard for finding lack of written description in such circumstance is where the art is unpredictable such that one of

ordinary skill in the art could not predict operability for the invention using species other than those specifically exemplified, such as in the biotech area. But the PTO has the burden of proof as to the unpredictability allegation (see, e.g., *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)) and no evidence is provided in the instant case to meet this burden. To the contrary, the Background of the specification refers to known art relating to methods for local administration of drugs for other effects and also to general administration of drugs to reduce normal tissue, generally. Applicants' invention distinguishes from these known methods in that it involves localized administration of a controlled release drug formulation for the local elimination or reduction of normal, but undesired, tissue. This patentably distinguishes the prior art but the prior art (given applicants advance thereto) is indicative to one of ordinary skill in the art that, given applicants' disclosure, there would be a predictability to the operability of applying any of a variety of known (or not yet known) drugs by local administration of a controlled release drug formulation for the local elimination or reduction of normal, but undesired, tissue. The novelty of applicants invention – in its broadest sense – does not reside in the type of tissue being removed (except that is normal but undesired tissue) or in the drug being used to effect such removal but rather in the fact that this is done by local administration in a controlled release drug formulation for the local elimination of the tissue. Thus, the breadth in encompassing a variety of tissues and drugs does not support a lack of written description of the invention because the particular type of normal but undesired tissue and the particular type of drug is not applicants' invention.

To make a more simplified example, assume the claim were to a method of treating a disease by administering a drug using a syringe with a novel design. The fact that applicants do not describe all the types of drugs which could be used in the syringe or all the types of

diseases which the injection could be used for does not mean that written description of the invention is lacking. The situation is analogous here.

For the above reasons, applicants respectfully submit that the instant claims have adequate written description and the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

The Rejection under 35 U.S.C. §102

The rejection of claims 1-3, 5, 6, 9-12, 14 and 17 under 35 U.S.C. §102, as being anticipated by Goldenberg (WO 98/46211) is respectfully traversed.

Goldenberg is directed to sustained-release formulations of alginate beads co-precipitated with a biologically active agent. Goldenberg discloses a wide variety of drugs as the biologically active agent. Goldenberg also discloses methods for treating indications with the sustained-release formulations containing the biologically active agent; see, e.g., page 7, lines 16-19. The methods for using the formulations are further discussed at pages 14-18. Using formulations which contain an anti-obesity drug is discussed, among others.

Goldenberg does not disclose a method wherein the sustained-release formulation is administered to the patient "by injection at a local area containing the undesired tissue such that the undesired tissue in the local area is eliminated or reduced." Compare instant claim 1. Goldenberg discloses only methods wherein the patient is subject to a general effect by the drug. For example, in all the embodiments referring to Goldenberg's anti-obesity methods, the results are discussed in terms of overall weight of the patient (or animal model, see, e.g, page 22) and not in terms of the loss of tissue in any particular local area, particularly not in the local area into which the drug is administered. Although Goldenberg does teach that its formulations may be administered by injection, it does not provide any disclosure that such

injection results in elimination or reduction of the normal but undesired tissue in the local area of the injection.

In order to anticipate, "[e]very element of the claim must be literally present, arranged as in the claim," see, e.g., Richardson v. Suzuki Motor Co., 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Goldenberg is lacking the element recited in applicants' claims that the controlled release formulation be administered "by injection at a local area containing the undesired tissue such that the undesired tissue in the local area is eliminated or reduced." Accordingly, Goldenberg cannot anticipate the instant claims and the rejection under 35 U.S.C. §102 should be withdrawn.

The First Rejection under 35 U.S.C. §103

The rejection of claims 1-3, 5-12, 14 and 17 under 35 U.S.C. §103, as being obvious over Goldenberg is respectfully traversed.

The discussion of Goldenberg above in connection with the traversal of the 35 U.S.C. §102 rejection is incorporated herein by reference. To summarize, Goldenberg fails to disclose a method wherein the controlled release formulation is injected at a local area containing the normal but undesired tissue and the normal undesired tissue in the local area is eliminated or reduced. Applicants urge that Goldenberg also fails to suggest modifying its method to meet the local effect element of the instant claims.

Goldenberg provides no teachings which give any hint to one of ordinary skill in the art that a controlled release formulation could be injected at a local area to eliminate or reduce normal but undesired tissue in that local area. To the contrary, all the teachings in Goldenberg relate to administration of a sustained-release formulation to achieve general effects on the patient, for example, overall weight loss. There is no suggestion that a specific

local area of the injection could be targeted. A general weight loss effect taught by Goldenberg suggests to one of ordinary skill in the art that the weight loss is relatively evenly distributed in the patient and, thus, is not suggestive of the elimination or reduction of tissue targeted to the local area of injection.

For the above reasons, it is urged that Goldenberg fails to render the claimed invention obvious to one of ordinary skill in the art. Thus, the rejection under 35 U.S.C. §103 should be withdrawn.

The Second Rejection under 35 U.S.C. §103

The rejection of claims 1-3, 5, 6, 9-12 and 14-17 under 35 U.S.C. §103, as being obvious over Goldenberg further in view of any of the Hutchinson, Ogawa or Johnson articles is respectfully traversed.

The discussion of Goldenberg above in connection with the traversal of the 35 U.S.C. §102 and §103 rejections is incorporated herein by reference. To summarize, Goldenberg fails to disclose or suggest a method wherein the controlled release formulation is injected at a local area containing the normal but undesired tissue and the normal undesired tissue in the local area is eliminated or reduced. Applicants urge that the Hutchinson, Ogawa and/or Johnson references fail to make up for this deficiency of Goldenberg. Their combination with Goldenberg also fails to suggest modifying the method to meet the local effect element of the instant claims.

Hutchinson, Ogawa and Johnson were cited for their teachings regarding specific types of formulations for sustained-release effect and for their teachings regarding the duration of such effect. However, like Goldenberg, all of these references teach administration of sustained-release formulations of drugs to provide a general effect on the

patient. Thus, no combination of Goldenberg with any of these references would suggest a method wherein a controlled release formulation is injected at a local area to reduce or eliminate normal but undesired tissue at the local area of the injection.

Accordingly, this rejection under 35 U.S.C. §103 should also be withdrawn.

The Third Rejection under 35 U.S.C. §103

The rejection of claims 1-3, 5, 6, 9-12, 14, 17, 24 and 25 under 35 U.S.C. §103, as being obvious over Goldenberg in view of Silvestri (U.S. Patent No. 5,126,147) is respectfully traversed.

The discussion of Goldenberg above in connection with the traversal of the 35 U.S.C. §102 and §103 rejections is incorporated herein by reference. To summarize, Goldenberg fails to disclose or suggest a method wherein the controlled release formulation is injected at a local area containing the normal but undesired tissue and the normal undesired tissue in the local area is eliminated or reduced. Applicants urge that the Silvestri reference fails to make up for this deficiency of Goldenberg. Its combination with Goldenberg also fails to suggest modifying the method to meet the local effect element of the instant claims.

Silvestri was cited for its teachings regarding multiphasic controlled release systems. However, like Goldenberg, Silvestri relates only to administration of sustained-release formulations of drugs to provide a general effect on the patient. Thus, the combination of Goldenberg with Silvestri fails to suggest a method wherein a controlled release formulation is injected at a local area to reduce or eliminate normal but undesired tissue at the local area of the injection.

Accordingly, this rejection under 35 U.S.C. §103 should also be withdrawn.

The Fourth Rejection under 35 U.S.C. §103

The rejection of claims 1-3, 5, 6, 9-12, 14, 17 and 24-26 under 35 U.S.C. §103, as being obvious over Goldenberg and Silvestri, further in view of the Merwin article is respectfully traversed.

The discussion of Goldenberg and Silvestri above is incorporated herein by reference. To summarize, the combination of Goldenberg and Silvestri fails to disclose or suggest a method wherein the controlled release formulation is injected at a local area containing the normal but undesired tissue and the normal undesired tissue in the local area is eliminated or reduced. Applicants urge that the Merwin fails to make up for this deficiency of the Goldenberg/Silvestri combination. Merwin also fails to suggest modifying the method to meet the local effect element of the instant claims.

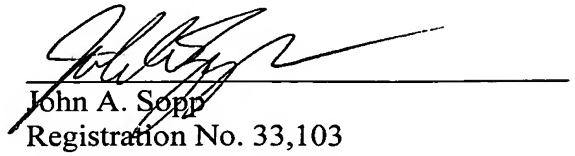
Merwin was cited for its teachings regarding use of an aFGF protein as an anti-angiogenic agent. However, like Goldenberg and Silvestri, Merwin relates only to administration of sustained-release formulations of drugs to provide a general effect on the patient. Thus, the combination of Merwin with Goldenberg and Silvestri fails to suggest a method wherein a controlled release formulation is injected at a local area to reduce or eliminate normal but undesired tissue at the local area of the injection. Even if the Merwin protein were used together with TNF, there is no suggestion of such combined use for a local tissue reduction effect.

Accordingly, this rejection under 35 U.S.C. §103 should also be withdrawn.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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